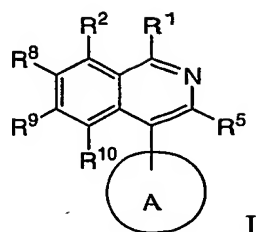


WHAT IS CLAIMED IS:

1. A compound of formula I



or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

- a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO<sub>2</sub>,
- 3) CN,
- 4) CR<sup>46</sup>=C(R<sup>47</sup>R<sup>48</sup>)<sub>2</sub>,
- 5) C≡C R<sup>46</sup>,
- 6) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>OR<sup>46</sup>,
- 7) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 8) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> C(O)R<sup>46</sup>,
- 9) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> C(O)OR<sup>46</sup>,
- 10) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>46</sup>,
- 11) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> S(O)<sub>0-2</sub>R<sup>61</sup>,
- 12) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> S(O)<sub>0-2</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 13) OS(O)<sub>0-2</sub>R<sup>61</sup>,
- 14) N(R<sup>46</sup>)C(O)R<sup>47</sup>,
- 15) N(R<sup>46</sup>)S(O)<sub>0-2</sub>R<sup>61</sup>,
- 16) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>,
- 17) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>OR<sup>47</sup>,
- 18) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)(CR<sup>k</sup>R<sup>l</sup>)<sub>s</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),
- 19) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>61</sup>,
- 20) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>47</sup>R<sup>48</sup>),
- 21) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),

22) oxo,

b) a heteroaryl ring selected from the group consisting of

a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O and S, and

a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO<sub>2</sub>,

3) CN,

4) CR<sup>46</sup>=C(R<sup>47</sup>R<sup>48</sup>)<sub>2</sub>,

5) C≡C R<sup>46</sup>,

6) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>OR<sup>46</sup>,

7) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>R<sup>47</sup>),

8) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> C(O)R<sup>46</sup>,

9) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> C(O)OR<sup>46</sup>,

10) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>46</sup>,

11) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> S(O)<sub>0-2</sub>R<sup>61</sup>,

12) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub> S(O)<sub>0-2</sub>N(R<sup>46</sup>R<sup>47</sup>),

13) OS(O)<sub>0-2</sub>R<sup>61</sup>,

14) N(R<sup>46</sup>)C(O)R<sup>47</sup>,

15) N(R<sup>46</sup>)S(O)<sub>x</sub>R<sup>61</sup>,

16) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>,

17) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>OR<sup>47</sup>,

18) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)(CR<sup>k</sup>R<sup>l</sup>)<sub>s</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),

19) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>61</sup>,

20) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>47</sup>R<sup>48</sup>),

21) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>), or

22) oxo, or

c) a 4-, 5- or 6-membered heterocyclic ring containing 1 or 2 nitrogen atoms, unsubstituted, mono-substituted or di-substituted with C<sub>1</sub>-C<sub>6</sub> alkyl;

Y is CH<sub>2</sub>, NR<sup>53</sup>, NC(O)R<sup>53</sup>, S(O)<sub>0-2</sub> or O;

G is H<sub>2</sub> or O;

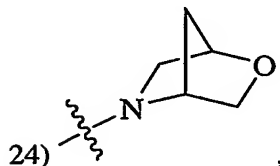
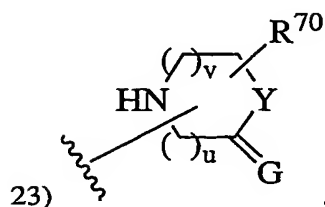
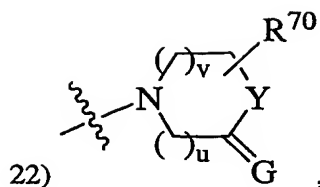
R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>e</sup>, R<sup>f</sup>, R<sup>g</sup>, R<sup>h</sup>, R<sup>i</sup>, R<sup>j</sup>, R<sup>k</sup>, and R<sup>l</sup> are independently selected from the group consisting of:

- 5                   1) hydrogen,
- 2) C<sub>1</sub>-C<sub>6</sub> alkyl,
- 3) halogen,
- 4) aryl,
- 5) R<sup>80</sup>,
- 10               6) C<sub>3</sub>-C<sub>10</sub> cycloalkyl, and
- 7) OR<sup>4</sup>,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R<sup>7</sup>, disubstituted with R<sup>7</sup> and R<sup>15</sup>, trisubstituted with R<sup>7</sup>, R<sup>15</sup> and R<sup>16</sup>, or tetrasubstituted with R<sup>7</sup>, R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup>;

R<sup>1</sup> is independently selected from:

- 15               1) hydrogen,
- 2) halogen,
- 3) NO<sub>2</sub>,
- 4) CN,
- 5) CR<sup>40</sup>=C(R<sup>41</sup>R<sup>42</sup>),
- 20               6) C≡CR<sup>40</sup>,
- 7) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>OR<sup>40</sup>,
- 8) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>R<sup>41</sup>),
- 9) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>C(O)R<sup>40</sup>,
- 10) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>C(O)OR<sup>40</sup>,
- 25               11) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>R<sup>40</sup>,
- 12) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>S(O)<sub>0-2</sub>R<sup>6</sup>,
- 13) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>S(O)<sub>0-2</sub>N(R<sup>40</sup>R<sup>41</sup>),
- 14) OS(O)<sub>0-2</sub>R<sup>6</sup>,
- 15) N(R<sup>40</sup>)C(O)R<sup>41</sup>,
- 30               16) N(R<sup>40</sup>)S(O)<sub>0-2</sub>R<sup>6</sup>,
- 17) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)R<sup>6</sup>,
- 18) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)R<sup>6</sup>OR<sup>41</sup>,
- 19) (CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)(CR<sup>c</sup>R<sup>d</sup>)<sub>t</sub>C(O)N(R<sup>41</sup>R<sup>42</sup>),
- 20) N(R<sup>40</sup>)(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>R<sup>6</sup>,
- 35               21) N(R<sup>40</sup>)(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>41</sup>R<sup>42</sup>),



25)  $(\text{CR}^a\text{R}^b)_n\text{C}(\text{O})\text{N}(\text{R}^{41}\text{R}^{42})$ , and

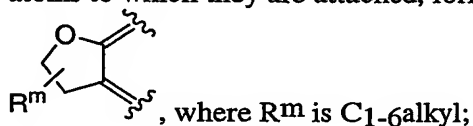
26) a 4-, 5-, or 6-membered heterocyclic ring containing 1 nitrogen atom, unsubstituted, or mono-, di- or tri-substituted with -OH;

$\text{R}^2$ ,  $\text{R}^8$ ,  $\text{R}^9$  and  $\text{R}^{10}$  are independently selected from:

- 1) hydrogen,
- 2) halogen,
- 3)  $\text{NO}_2$ ,
- 4)  $\text{CN}$ ,
- 5)  $\text{CR}^{43}=\text{C}(\text{R}^{44}\text{R}^{45})$ ,
- 6)  $\text{C}\equiv\text{CR}^{43}$ ,
- 7)  $(\text{CR}^e\text{R}^f)_p\text{OR}^{43}$ ,
- 8)  $(\text{CR}^e\text{R}^f)_p\text{N}(\text{R}^{43}\text{R}^{44})$ ,
- 9)  $(\text{CR}^e\text{R}^f)_p\text{C}(\text{O})\text{R}^{43}$ ,
- 10)  $(\text{CR}^e\text{R}^f)_p\text{C}(\text{O})\text{OR}^{43}$ ,
- 11)  $(\text{CR}^e\text{R}^f)_p\text{R}^{43}$ ,
- 12)  $(\text{CR}^e\text{R}^f)_p\text{S}(\text{O})_{0-2}\text{R}^{60}$ ,
- 13)  $(\text{CR}^e\text{R}^f)_p\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{43}\text{R}^{44})$ ,
- 14)  $\text{OS}(\text{O})_{0-2}\text{R}^{60}$ ,
- 15)  $\text{N}(\text{R}^{43})\text{C}(\text{O})\text{R}^{44}$ ,

- 16)  $N(R^{43})S(O)_{0-2}R^{60}$ ,  
 17)  $(CReRf)_pN(R^{43})R^{60}$ ,  
 18)  $(CReRf)_pN(R^{43})R^{60}OR^{44}$ ,  
 19)  $(CReRf)_pN(R^{43})(CReRh)_qC(O)N(R^{44}R^{45})$ ,  
 20)  $N(R^{43})(CReRf)_pR^{60}$ ,  
 21)  $N(R^{43})(CReRf)_pN(R^{44}R^{45})$ , and  
 22)  $(CReRf)_pC(O)N(R^{43}R^{44})$ ,

or  $R^2$  and  $R^8$  are independently as defined above, and  $R^9$  and  $R^{10}$ , together with the atoms to which they are attached, form the ring



$R^4, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52}$ , and  $R^{53}$  are independently selected from:

- 1) hydrogen,  
 2)  $C_1-C_6$  alkyl,  
 3)  $C_3-C_{10}$  cycloalkyl,  
 4) aryl,  
 5)  $R^{81}$ ,  
 6)  $CF_3$ ,  
 7)  $C_2-C_6$  alkenyl, and  
 8)  $C_2-C_6$  alkynyl,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with  $R^{18}$ , di-substituted with  $R^{18}$  and  $R^{19}$ , tri-substituted with  $R^{18}, R^{19}$  and  $R^{20}$ , or tetra-substituted with  $R^{18}, R^{19}, R^{20}$  and  $R^{21}$ ;

$R^5$  is independently selected from:

- 1) hydrogen,  
 2) halogen,  
 3) CN,  
 4)  $C(O)N(R^{49}R^{50})$ ,  
 5)  $C(O)OR^{49}$ ,  
 6)  $S(O)_{0-2}N(R^{49}R^{50})$ ,  
 7)  $S(O)_{0-2}R^{62}$ ,  
 8)  $C_1-C_6$  alkyl,  
 9)  $C_3-C_{10}$  cycloalkyl,  
 10)  $R^{82}$ ,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R<sup>22</sup>, di-substituted with R<sup>22</sup> and R<sup>23</sup>, tri-substituted with R<sup>22</sup>, R<sup>23</sup> and R<sup>24</sup>, or tetra-substituted with R<sup>22</sup>, R<sup>23</sup>, R<sup>24</sup> and R<sup>25</sup>;

R<sup>6</sup>, R<sup>60</sup>, R<sup>61</sup>, R<sup>62</sup> and R<sup>63</sup> are independently selected from:

- 1) C<sub>1</sub>-C<sub>6</sub> alkyl,
- 2) aryl,
- 3) R<sup>83</sup>, and
- 4) C<sub>3</sub>-C<sub>10</sub> cycloalkyl;

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R<sup>26</sup>, di-substituted with R<sup>26</sup> and R<sup>27</sup>, tri-substituted with R<sup>26</sup>, R<sup>27</sup> and R<sup>28</sup>, or tetra-substituted with R<sup>26</sup>, R<sup>27</sup>, R<sup>28</sup> and R<sup>29</sup>;

R<sup>7</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>24</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>27</sup>, R<sup>28</sup>, R<sup>29</sup>, and R<sup>70</sup> are independently selected from:

- 1) C<sub>1</sub>-C<sub>6</sub> alkyl,
- 2) halogen,
- 3) OR<sup>51</sup>,
- 4) CF<sub>3</sub>,
- 5) aryl,
- 6) C<sub>3</sub>-C<sub>10</sub> cycloalkyl,
- 7) R<sup>84</sup>,
- 8) S(O)<sub>0-2</sub>N(R<sup>51</sup>R<sup>52</sup>),
- 9) C(O)OR<sup>51</sup>,
- 10) C(O)R<sup>51</sup>,
- 11) CN,
- 12) C(O)N(R<sup>51</sup>R<sup>52</sup>),
- 13) N(R<sup>51</sup>)C(O)R<sup>52</sup>,
- 14) S(O)<sub>0-2</sub>R<sup>63</sup>,
- 15) NO<sub>2</sub>, and
- 16) N(R<sup>51</sup>R<sup>52</sup>);

R<sup>80</sup>, R<sup>81</sup>, R<sup>82</sup>, R<sup>83</sup> and R<sup>84</sup> are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting or N, O or S;

n, p, q, r, s and t are independently 0, 1, 2, 3, 4, 5 or 6;

u is 0, 1 or 2; and

v is 0, 1 or 2.

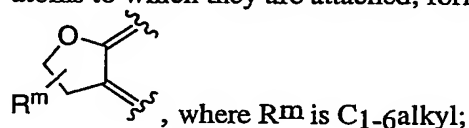
2. A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

5 A is a) an aryl ring selected from phenyl, unsubstituted or substituted as in Claim 1, b) a heteroaryl ring, unsubstituted or substituted as in Claim 1, selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole, benzothiazole, and benzoxadiazole, or c) a 4-, 5- or 6-membered heterocyclic ring as defined in Claim 1;

R<sup>2</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of:

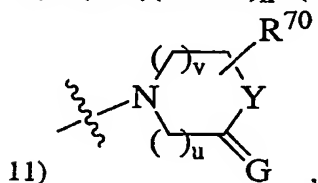
- 10 1) hydrogen,  
2) halogen,  
3) OR<sup>43</sup>, and  
4) (CR<sup>e</sup>R<sup>f</sup>)<sub>p</sub>R<sup>43</sup>,

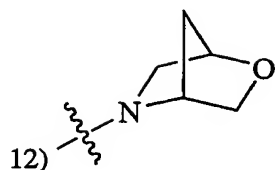
or R<sup>2</sup> and R<sup>8</sup> are independently as defined above, and R<sup>9</sup> and R<sup>10</sup>, together with the  
15 atoms to which they are attached, form the ring



R<sup>1</sup> is independently selected from:

- 20 1) hydrogen,  
2) halogen,  
3) CN,  
4) OR<sup>40</sup>,  
5) N(R<sup>40</sup>R<sup>41</sup>),  
6) C(O)OR<sup>40</sup>,  
7) R<sup>81</sup>,  
25 8) S(O)<sub>0-2</sub>R<sup>6</sup>,  
9) N(R<sup>40</sup>)(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>R<sup>6</sup>, wherein R<sup>6</sup> = R<sup>83</sup>,  
10) N(R<sup>40</sup>)(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>41</sup>R<sup>42</sup>),





12) ,  
 13) C(O)N(R<sup>41</sup>R<sup>42</sup>), and

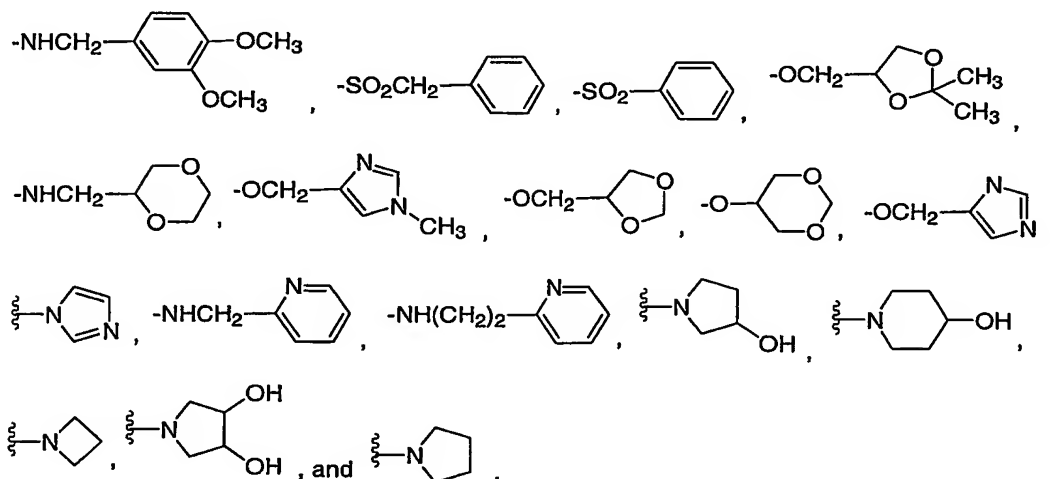
14) a 4-, 5-, or 6-membered heterocyclic ring containing 1 nitrogen atom, unsubstituted, or mono-, di- or tri-substituted with -OH.

5

3. A compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein R<sup>2</sup>, R<sup>8</sup>, and R<sup>10</sup> are independently selected from hydrogen and halogen, and R<sup>9</sup> is OCH<sub>3</sub> or OCHF<sub>2</sub>.

4. A compound of Claim 3, or a pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> is selected from the group consisting of hydrogen, -SCH<sub>3</sub>, -SO<sub>2</sub>CH<sub>3</sub>, -NH(CH<sub>2</sub>)<sub>3</sub>OH, -NH(CH<sub>2</sub>)<sub>2</sub>OH, -NH(CH<sub>2</sub>)<sub>2</sub>OCH<sub>3</sub>, -NH(CH<sub>2</sub>)<sub>3</sub>OCH<sub>3</sub>, -NH(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub>, -NH<sub>2</sub>, -SO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, -CN, Cl, -OCH<sub>3</sub>, -OCH<sub>2</sub>CHCH<sub>2</sub>, -OCH<sub>2</sub>CH(OH)CH<sub>2</sub>OH, -NHCH<sub>2</sub>CHCH<sub>2</sub>, -CH<sub>3</sub>, -CH<sub>2</sub>CH<sub>2</sub>OH, -O(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>, -O(CH<sub>2</sub>)<sub>2</sub>CH(OH)(CH<sub>2</sub>OH), -NHCH(CH<sub>2</sub>OH)<sub>2</sub>, -NHCH<sub>2</sub>CH(OH)CH<sub>2</sub>OH, -NH(CH<sub>2</sub>)<sub>2</sub>CH(OH)CH<sub>2</sub>OH,

15



5. A compound of Claim 4, or a pharmaceutically acceptable salt thereof, wherein A is selected from the group consisting of

- 20 1) phenyl, wherein any stable ring atom is unsubstituted or substituted with halogen,  
 2) pyridinyl, wherein any stable C ring atom is unsubstituted or substituted with halogen,



- 3) indolyl, wherein any stable C or N ring atom is unsubstituted or substituted with halogen, and  
 4) a heterocyclic ring selected from the group consisting of pyrrolidine, piperidine, piperazine, and azetidine, unsubstituted, mono-substituted or di-substituted with C<sub>1</sub>-C<sub>6</sub> alkyl.

- 5                    6.        A compound of Claim 5, or a pharmaceutically acceptable salt thereof, wherein R<sup>5</sup> is selected from the group consisting of CN and C<sub>1</sub>-C<sub>6</sub> alkyl, wherein said alkyl is unsubstituted, mono-substituted with R<sup>22</sup>, di-substituted with R<sup>22</sup> and R<sup>23</sup>, tri-substituted with R<sup>22</sup>, R<sup>23</sup> and R<sup>24</sup>, or tetra-substituted with R<sup>22</sup>, R<sup>23</sup>, R<sup>24</sup> and R<sup>25</sup>.
- 10                   7.        A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of  
 [(6-methoxy-4-phenylisoquinolin-3-yl)methyl]dimethylamine,  
 1-(1-chloro-6-methoxy-4-phenylisoquinolin-3-yl)-N,N-dimethylmethanamine,  
 {[6-methoxy-1-(methylthio)-4-phenylisoquinolin-3-yl)methyl}dimethylamine,  
 15 [6-methoxy-1-(methylsulfonyl)-4-phenylisoquinolin-3-yl)methyl(dimethyl)amine oxide,  
 1-[6-methoxy-1-(methylsulfonyl)-4-phenylisoquinolin-3-yl]-N,N-dimethylmethanamine,  
 3-[(dimethylamino)methyl]-6-methoxy-4-phenylisoquinoline-1-carbonitrile,  
 2,3-Dimethyl-6-methoxy-4-phenylisoquinolinium hydroxide,  
 6-methoxy-1-(2-methoxyethoxy)-3-methyl-4-phenylisoquinoline,  
 20 {3-[(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)oxy]propyl}amine,  
 2-[(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)amino]ethanol,  
 6-methoxy-3-methyl-1-(methylsulfonyl)-4-phenylisoquinoline,  
 6-methoxy-N-(2-methoxyethyl)-3-methyl-4-phenylisoquinolin-1-amine,  
 N-(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)ethane-1,2-diamine,  
 25 6-methoxy-3-methyl-4-phenylisoquinoline,  
 N-(3,4-dimethoxybenzyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1-amine,  
 6-methoxy-3-methyl-4-phenylisoquinolin-1-amine,  
 1-(ethylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,

- 1-(benzylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,  
6-methoxy-3-methyl-4-phenyl-1-(phenylsulfonyl)isoquinoline,  
6-methoxy-3-methyl-4-phenylisoquinoline-1-carbonitrile,  
3-tert-butyl-6-methoxy-1-(2-methoxyethoxy)-4-phenylisoquinoline,  
5 1-chloro-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
6-methoxy-4-phenylisoquinoline-1,3-dicarbonitrile,  
1-(allyloxy)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
1-(2,3-dihydroxypropoxy)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
(allylamino)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
10 (+/-)-1-[(2,3-dihydroxypropyl)amino]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
1-[(2S)-2,3-dihydroxypropyl]amino}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
1-[(2R)-2,3-dihydroxypropyl]amino}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
(+/-)-1-[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]-6-methoxy-4-phenylisoquinoline-3-  
carbonitrile,  
15 1-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]methoxy}-6-methoxy-4-phenylisoquinoline-3-  
carbonitrile,  
1-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]methoxy}-6-methoxy-4-phenylisoquinoline-3-  
carbonitrile,  
1-[(2R)-2,3-dihydroxypropyl]oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
20 1-[(2S)-2,3-dihydroxypropyl]oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
(+/-)-1-[(2,3-dihydroxypropyl]oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
1-[(3R)-3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
1-[(3S)-3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
(+/-)-1-[3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
25 1-[cis-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

- 6-methoxy-4-phenyl-1-pyrrolidin-1-ylisoquinoline-3-carbonitrile,  
6-methoxy-1-(methylsulfonyl)-4-phenylisoquinoline-3-carbonitrile,  
6-methoxy-4-phenylisoquinoline-3-carbonitrile,  
1,6-dimethoxy-4-phenylisoquinoline-3-carbonitrile,
- 5 1-chloro-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
4-(3-fluorophenyl)-6-methoxy-1-methylisoquinoline-3-carbonitrile,  
4-(3-fluorophenyl)-1-[(2-hydroxyethyl)amino]-6-methoxyisoquinoline-3-carbonitrile,  
1-amino-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 10 4-(3-fluorophenyl)-1-[(3-hydroxypropyl)amino]-6-methoxyisoquinoline-3-carbonitrile,  
1-(but-3-enyloxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
(+/-)-1-(2,3-dihydroxypropoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
1-[(2R)-2,3-dihydroxypropoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
1-[(2S)-2,3-dihydroxypropoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 15 (+/-)-1-(3,4-dihydroxybutoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
(+/-)-1-[(3R)-3,4-dihydroxybutoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
1-[(3S)-3,4-dihydroxybutoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,  
(+/-)-1-[(1,4-dioxan-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-  
carbonitrile,
- 20 1-[(1,4-dioxan-(2R)-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-  
carbonitrile,  
1-[(1,4-dioxan-(2S)-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-  
carbonitrile,  
4-(3-fluorophenyl)-6-methoxy-1-[(1-methyl-1H-imidazol-4-yl)methoxy]isoquinoline-3-
- 25 carbonitrile,

- (+/-)-1-(1,3-dioxolan-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 1-(1,3-dioxolan-(4R)-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 1-(1,3-dioxolan-(4S)-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 5 1-(1,3-dioxan-5-yloxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 4-(3-fluorophenyl)-1-{[2-hydroxy-1-(hydroxymethyl)ethyl]amino}-6-methoxyisoquinoline-3-carbonitrile,
- 4-(3-fluorophenyl)-1-(1H-imidazol-5-ylmethoxy)-6-methoxyisoquinoline-3-carbonitrile,
- 1-[[{(2R)-2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
- 10 carbonitrile,
- 1-[[{(2S)-2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- (+/-)-1-[[2,3-dihydroxypropyl]amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 15 1-(1H-imidazol-1-yl)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
- 6-methoxy-4-phenyl-1-[(pyridin-2-ylmethyl)amino]isoquinoline-3-carbonitrile,
- 6-methoxy-4-phenyl-1-[(2-pyridin-2-ylethyl)amino]isoquinoline-3-carbonitrile,
- (+/-)-1-[(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 20 1-[(3R)-(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 1-[(3S)-(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 1-chloro-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
- 25 4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

(+/-)-1-[(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-[(2S)-(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

5 1-[(2R)-(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

(+/-)-6-(difluoromethoxy)-1-{[2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

10 6-(difluoromethoxy)-1-[[2,3-dihydroxypropyl]amino]-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

6-(difluoromethoxy)-1-[[2,3-dihydroxypropyl]amino]-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

(+/-)-6-(difluoromethoxy)-1-{[2,3-dihydroxypropyl]oxy}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

15 6-(difluoromethoxy)-1-[[2,3-dihydroxypropyl]oxy]-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

6-(difluoromethoxy)-1-[[2,3-dihydroxypropyl]oxy]-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

1-(4-hydroxypiperidin-1-yl)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

20 1-azetidin-1-yl-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

(+/-)-1-[trans-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-[(3R,4R)-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-[(3S,4S)-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile, and

6-methoxy-N-(3-methoxypropyl)-3-methyl-4-phenylisoquinolin-1-amine.

25

8. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by  $K_v1.5$  inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting  $K_v1.5$ .

5 9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10. A method of Claim 9, wherein the cardiac arrhythmia is atrial fibrillation.

10 11. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

12. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by  $K_v1.5$  inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting  $K_v1.5$ .

15 13. A method of Claim 12, wherein the condition is cardiac arrhythmia.

14. A method of Claim 13, wherein the cardiac arrhythmia is atrial fibrillation.

20 15. A method of Claim 13, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

16. A method of Claim 12, wherein the condition is a thromboembolic event.

25 17. A method of Claim 16, wherein the thromboembolic event is a stroke.

18. A method of Claim 12, wherein the condition is congestive heart failure.

30 19. A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim 1 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

21. A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta  
5 blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

10 22. A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.